Chemistry of Heterocyclic Compounds, Vol. 33, No. 9, 1997

ISOIMIDES OF BENZENE-1,2-DICARBOXYLIC ACID AND NAPTHALENE-1,8-DICARBOXYLIC ACID. SUITABLE CONDITIONS FOR PREPARATION

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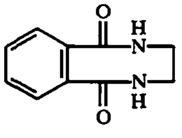
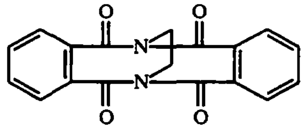
N-Arylisophthalimides are formed in an aprotic solvent at 20°C from equivalent quantities of phthaloyl chloride and an arylamine in the presence of not less than 1 mole of a dehydrochlorinating reagent. N-Nitrophenylisonaphthalimides were obtained by the reaction of an equimolar mixture of naphthaloyl chloride and nitroanilines in boiling toluene.

In 1892 it was suggested that an isophthalimide heterocycle might be an intermediate in the synthesis of 2-cyanobenzoic acid by the reaction of symmetrical phthaloyl chloride with ammonia [1]. N-Methylisophthalimide was later obtained by the reaction of phthalic anhydride with methylamine and dehydration of the resulting methylphthalamic acid with thionyl chloride [2]. A series of alkylisophthalimides was also obtained by the reaction of equimolar quantities of symmetrical phthaloyl chloride and primary amines in the presence of 4 moles of triethylamine to aid cyclization [3]. This [2, 3] indirectly confirmed the hypothesis of [1].

Attempts at a direct proof of isophthalimide formation by the reaction of phthaloyl chloride with primary amines alone in a molar ratio 1:3 [4] proved to be pointless, as was shown in [5]. The data of [5] indicated the impossibility of a direct synthesis of isoimides according to the hypothesis of [1]. Fragmentary data on the instability of isoimides both thermally [6], and also in the presence of basic reagents, consisted of a string of inaccurate assignments of the products from the reaction of ortho and peri dicarboxylic acid chlorides with primary diamines as a benzodiazacine (I) [7], a dibenzodiazecine (II) [8, 9], and a naphthalimide of symmetrical structure (III) [10].


I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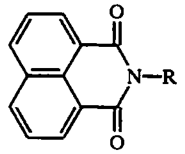
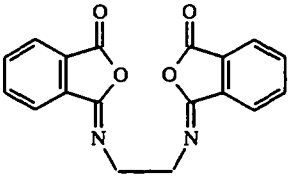

IIIa-c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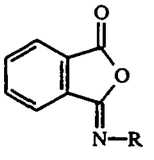
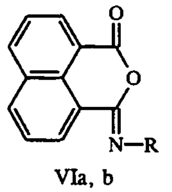

Va, b


VIa, b

III a R = C_6H_5, b R = 3-$NO_2C_6H_4$, c R = 4-$NO_2C_6H_4$; V a R = C_6H_5, b R = 4-BrC_6H_4;
VI a R = 3-$NO_2C_6H_4$, b R = 4-$NO_2C_6H_4$

Physicochemical Institute for the Protection of Man and the Environment, Ministry of Education and Academy of Sciences of Ukraine, Odessa 270100. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1251-1253, September, 1997. Original article submitted January 13, 1997.

The inaccuracy of the structural assignments of compounds (I) and (II) was discussed in [11] and of structures (IIIa-c) in [12] and was confirmed by an x-ray structural analysis of diisophthalimidoethane (IV) in [13].

The aim of the present work was to clarify the minimum conditions required for the synthesis of isoimides, using isophthalimide and isonaphthalimide heterocycles as examples.

The isophthalimides (Va, b) were obtained by the direct reaction of symmetrical and unsymmetrical phthaloyl chlorides with primary arylamines in a molar ratio of 1:2, thus confirming directly the hypothesis of [1]. The ratio of reactants, not obvious from the data of [4, 5], the use of symmetrical and unsymmetrical phthaloyl chlorides, and the assessment of using sterically hindered primary tert-alkylamines in this reaction [3, 7], enabled suitable conditions of forming isophthalimides to be formulated. For their synthesis it is satisfactory to stir equimolar quantities of the structure-forming reactants, viz. phthaloyl chloride and the primary amine, at 20°C in an aprotic solvent in the presence of not less than 1 mole of a dehydrochlorinating reagent, such as a tertiary or primary amine. A primary amine must be present in no more than 1 mole in view of the formation of symmetrical phthalimides and phthaldiamides according to [5]. These same conditions are suitable for the synthesis of isonaphthalimides, particularly N-phenylisonaphthalimide [12].

We reacted an equimolar mixture of the structure-forming reactants, naphthaloyl chloride and nitroaniline, in boiling toluene, the conditions maximally favoring the synthesis of symmetrical imides [14], and obtained N-nitrophenylisonaphthalimides (VIa, b). This was to define more exactly the overall limits mentioned in [6] of the "instability" of isoimides connected with their tendency to isomerize, and to elucidate suitable conditions for forming isonaphthalimides. The identical results in the case described and in [12] refines ideas on the thermal stability of isoimides as a class [6], while emphasizing that even contact of a pair of structure-forming reactants in an equimolar mixture is a satisfactory condition for forming them and is a limiting example of the conditions of forming this function.

The data presented confirm directly the primary kinetic preference for O-acylation of amines and bring isoimides into the class of normal heterocyclic systems.

EXPERIMENTAL

The IR spectra were recorded on an IKS-29 instrument in KBr disks. Molecular ions (M^+) were recorded on a MAT 112 instrument at an ionization voltage of 70 eV with direct insertion of samples into the source. TLC was carried out on Silufol UV-254 plates in the system acetone–hexane (1:3 to 1:8) with visualization in UV light or with ninhydrin.

N-Arylisophthalimides (Va, b). A solution of aniline or 4-bromoaniline (0.2 mole) in benzene (100 ml) was added to a solution of symmetrical or unsymmetrical phthaloyl chloride (0.1 mole) in benzene (100 ml) at 20°C. The mixture was shaken, left for 15 min, and filtered. The filtrate was washed with 1% HCl (100 ml), then with water (2 × 100 ml), the benzene layer separated, filtered, evaporated to 60 ml at 60 mm Hg, cooled to 20°C, and the crystals of isophthalimide filtered off.

N-Phenylisophthalimide (Va) was obtained in 75% yield and had mp 120°C. Found, %: N 6.39. $C_{14}H_9NO_2$. Calculated, %: N 6.28. IR spectrum: 1805 (C=O); 1760 (C=N); 1230, 940 cm^{-1} (COC). M^+ 223.

N-(4-Bromophenyl)isophthalimide (Vb) was obtained in 70% yield and had mp 165°C. Found, %: N 6.50. $C_{14}H_8BrNO_2$. Calculated, %: N 6.64. IR spectrum: 1805 (C=O); 1710 (C=N); 1235, 930 cm^{-1} (COC). M^+ 301 and 303.

N-Nitrophenylisonaphthalimides (VIa, b). Naphthaloyl chloride (about 0.5 mmole) and 3-nitro- or 4-nitroaniline (about 0.5 mmole) each dissolved in toluene (250 ml) were mixed and the mixture heated for 5 h at 110°C. The toluene was distilled off, and isonaphthalimides (VIa, b) were crystallized from acetone.

N-(3-Nitrophenyl)isonaphthalimide (VIa) was obtained in 95% yield and had mp 220°C. Found, %: N 8.92. $C_{18}H_{10}N_2O_4$. Calculated, %: N 8.80. IR spectrum: 1760 (C=O); 1680 (C=N); 1050 cm^{-1} (COC). M^+ 318.

N-(4-Nitrophenyl)isonaphthalimide (VIb) was obtained in 97% yield and had mp 263°C. Found, %: N 8.70. $C_{18}H_{10}N_2O_4$. Calculated, %: 8.80. IR spectrum: 1760 (C=O); 1665 (C=N); 1050 cm^{-1} (COC). M^+ 318. The same isonaphthalimides (VIa, b) were also obtained in yields of 43 and 49% respectively at 20°C under the conditions of [12].

The symmetrical N-nitrophenylnaphthalimides required for comparison were obtained by the reaction of naphthalic anhydride with the appropriate nitroaniline by the method of [15]. N-(3-Nitrophenyl)naphthalimide (IIIb) was obtained in 60% yield and had mp 275°C. IR spectrum: 1725, 1690 cm^{-1} (C=O). M^+ 318. N-(4-Nitrophenyl)naphthalimide (IIIc) was obtained in 70% yield and had mp 310°C. IR spectrum: 1725, 1695 cm^{-1} (C=O). M^+ 318.

REFERENCES

1. M. S. Hoogewerff and W. A. van Dorp, Rec. Trav. Chim. Pay-Bas., **11**, 84 (1892).
2. M. S. Hoogewerff and W. A. van Dorp, Rec. Trav. Chim. Pay-Bas., **13**, 93 (1894).
3. E. V. Ganin, V. F. Anikin, and B. V. Rozynov, Khim. Geterotsikl. Soedin., No. 9, 1280 (1984).
4. M. Kuhara and M. Fukui, Am. Chem. J., **26**, 454 (1901).
5. M. S. Cherill, F. L. Shaeffer, and E. P. Shover, J. Am. Chem. Soc., **50**, 474 (1928).
6. D. H. R. Barton and W. D. Ollis (eds.), Comprehensive Organic Chemistry, Vol. 4, Pergamon, Oxford (1979), [Russian translation], Mir, Moscow (1983), p. 469.
7. H. Stetter, L. Marx-Moll, and H. Rutzen, Chem. Ber., **91**, 1775 (1958).
8. S. Wolf and S. K. Hasan, Can. J. Chem., **48**, 3566 (1970).
9. C. H. Gaozza, H. Grinberg, and S. Lamdan, J. Heterocycl. Chem., **9**, 883 (1972).
10. F. Mason, J. Chem. Soc., **125**, 2116 (1924).
11. E. V. Ganin, V. F. Anikin, and B. V. Rozynov, Zh. Org. Khim., **21**, 157 (1985).
12. E. V. Ganin, V. F. Makarov, and V. I. Nikitin, Khim. Geterotsikl. Soedin., No. 8, 1114 (1985).
13. Yu. A. Simonov, E. V. Ganin, and V. E. Zavodnik, Khim. Geterotsikl. Soedin., No. 10, 1320 (1987).
14. T. W. Evans and W. M. Dehn, J. Am. Chem. Soc., **51**, 3652 (1929).
15. B. A. Porai-Koshits, Zh. Obshch. Khim., **7**, 604 (1937).